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08/385,404

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Jan. 7, 95

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Kdm Rodriguez

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KEVIN RODRIGUEZ

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US006497872B1

(12) **United States Patent**
Weiss et al.(10) **Patent No.:** US 6,497,872 B1
(45) **Date of Patent:** Dec. 24, 2002(54) **NEURAL TRANSPLANTATION USING
PROLIFERATED MULTIPOTENT NEURAL
STEM CELLS AND THEIR PROGENY**(75) **Inventors:** Samuel Weiss, Alberta (CA); Brent
Reynolds, Alberta (CA); Joseph P.
Hammang, Barrington, RI (US); E.
Edward Baetge, Barrington, RI (US)(73) **Assignee:** NeuroSpheres Holdings Ltd., Calgary
(CA)(*) **Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.(21) **Appl. No.:** 08/486,313(22) **Filed:** Jun. 7, 1995**Related U.S. Application Data**(63) Continuation-in-part of application No. 08/270,412, filed on
Jul. 5, 1994, now abandoned, which is a continuation of
application No. 07/726,812, filed on Jul. 8, 1991, now
abandoned, application No. 08/486,313, which is a continu-
ation-in-part of application No. 08/385,404, filed on Feb. 7,
1995, now abandoned, which is a continuation of application
No. 07/961,813, filed on Oct. 16, 1992, now abandoned,
which is a continuation-in-part of application No. 07/726,
812, application No. 08/486,313, which is a continuation-
in-part of application No. 08/359,945, filed on Dec. 20,
1994, now abandoned, which is a continuation of application
No. 08/221,655, filed on Apr. 1, 1994, now abandoned,
which is a continuation of application No. 07/967,622, filed
on Oct. 28, 1992, now abandoned, which is a continuation-
in-part of application No. 07/726,812, filed on Jul. 8, 1991,
now abandoned, application No. 08/486,313, which is a
continuation-in-part of application No. 08/376,062, filed on
Jan. 20, 1995, now abandoned, which is a continuation of
application No. 08/010,829, filed on Jan. 29, 1993, now
abandoned, which is a continuation-in-part of application
No. 07/726,812, application No. 08/486,313, which is a
continuation-in-part of application No. 08/149,508, filed on
Nov. 9, 1993, now abandoned, which is a continuation-in-
part of application No. 07/726,812, application No. 08/486,
313, which is a continuation-in-part of application No. 08/311,
099, filed on Sep. 23, 1994, now abandoned, which is a
continuation-in-part of application No. 07/726,812,
application No. 08/486,313, which is a continuation-in-part
of application No. 08/338,730, filed on Nov. 14, 1994, now
abandoned, which is a continuation-in-part of application
No. 07/726,812.(51) **Int. Cl.⁷** A01N 63/00; A01N 65/00;
A61K 48/00(52) **U.S. Cl.** 424/93.1; 424/93.2; 424/93.21(58) **Field of Search** 424/93.1, 93.2,
424/93.21; 514/44(56) **References Cited****U.S. PATENT DOCUMENTS**4,753,635 A 6/1988 Sagen et al. 604/49
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Primary Examiner—Anne-Marie Baker(74) *Attorney, Agent, or Firm*—Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.; Ivor R. Elrifi, Esq.; Christine V.
Karnakis, Esq.(57) **ABSTRACT**The invention provides methods of transplanting multipo-
tent neural stem cell progeny to a host by obtaining a
population of cells derived from mammalian neural tissue
containing at least one multipotent CNS multipotent neural
stem cell; culturing the neural stem cell in a culture medium
containing one or more growth factors which induce mul-
tipotent neural stem cell proliferation; inducing proliferation
of the multipotent neural stem cell to produce neural stem
cell progeny which includes multipotent neural stem cell
progeny cells; and transplanting the multipotent neural stem
cell progeny to the host. Also provided are methods of
transplanting neural stem cell progeny to a host by obtaining
an in vitro cell culture containing CNS neural stem cells
where one or more cells in the culture (i) proliferates in a
culture medium supplemented with one or more mitogens,
(ii) retains the capacity for renewed proliferation, and (iii)
maintains the multipotential capacity, under suitable culture
conditions, to differentiate into neurons, astrocytes, and
oligodendrocytes; and transplanting the one or more cells to
the hose.**32 Claims, 3 Drawing Sheets**